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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,351	06/07/2002	Stace Lindsay	06727/008002	8638

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,351	LINDSAY ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 02, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *2,4,8,9 and 12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-7,10 and 11* is/are rejected.

7)☐ Claim(s) ____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/02/25006 has been entered.

No claim has been amended. Claims 1-20 are pending. Claims 2,4,8,9 and 12-20 are withdrawn as being drawn to a non-elected invention. Claims 1,3,5-7,10 and 11 are under consideration in the instant office action.

Claim Rejections - 35 USC § 112-1st paragraph

Claims 10 and 11 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a rHuAFP that is secreted in the milk of a transgenic non-human mammal wherein the non-human mammal is made by introducing the transgene into cells of an embryo and for a method of producing a rHuAFP that is secreted in the milk of a transgenic mouse wherein the mouse is made by introducing the transgene into cells of an embryo or into mouse ES cells, does not reasonably provide enablement for any such mammal made using any cell type. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is maintained for reasons of record set forth at pages 3-9 of the previous office action dated 03/22/2005.

Applicant's arguments have been fully considered and are not persuasive.

Claims 10 and 11 continue to encompass use of any transfected cell type to make an animal (see paragraph bridging pages 5-6 of the previous office action dated 03/22/2005). As set forth at pages 6-7 of the office action dated 03/22/2005, the state of the art at the time of filing held that it was routine to make transgenic non-human mammals using only fertilized oocytes or embryos that are transfected with a transgene, with the exception of transgenic mice, that can be made using totipotent ES cells. The state of the art of somatic cell nuclear transfer to generate a non-human animal was highly unpredictable as to the rate of success of making an animal, irrespective of transgene insertion or expression (see page 8 of the previous office action dated 03/22/2005).

Thus, the claims encompass use of any transfected cell to make a non-human mammal, which was not enabled by the specification or the art at the time of filing. Applicant has argued that several transgenic mice and goats that are capable of secreting rHuAFP into their milk have been made using techniques known in the art and taught in the specification. However, the specification does not clearly set forth that transgenic mammal, goats, mice or other species, that express rHuAFP in their milk were made by somatic cell nuclear transfer or were made by any means other than by pronuclear injection. Applicant asserts (Remarks, page 3, paragraph 3) that such animals were made using methods disclosed in the specification, wherein such methods include somatic cell nuclear transfer but also include pronuclear transfer and use of mouse ES cells. However, Applicant fails to indicate where the specification provides an enabling disclosure with regard to use of somatic cell nuclear transfer in making an animal transgenic. No more than the mere mention that nuclear transfer might be used to make a transgenic non-human

mammal that expresses rHuAFP in the milk has been found. The specification does not provide any guidance with respect to overcoming the underdeveloped nature and unpredictabilities associated with nuclear transfer (see page 5 of the office action dated 03/22/2005). The specification, for example, fails to provide any guidance with respect to what somatic cell types could be used to carry out the instant invention. The art has clearly demonstrated that the art of in vitro transformation of cells prior to nuclear transfer is limited with respect to what cells types can be used (see Thomson *et al.*, **Reprod. Supp.**, 61:495-508, 2003 and Polejaeva and Campbell, **Theriogenology**, 53:117-126, 2000).

The Stewart declaration under 37 CFR 1.132 filed 05/05/2006 is insufficient to overcome the rejection of claims 10 and 11 based upon the insufficiency of disclosure under 35 U.S.C. 112, first paragraph as set forth in the last Office action because: The goat, F093, appears to be the same goat disclosed at page 66 of related patent application 10/624,380. F093 appears to have made generated using pronuclear injection of a transgene encoding ng.HuAFP, not rHuAFP (see page 65 of '380). This, in light of Mr. Stewart's vague statement that a founder transgene goat was successfully generated "according to methods disclosed in the present specification" (see page 7, last paragraph of the Stewart Declaration), fails to establish that Applicant made a non-human mammal transgenic using a cell other than a mouse ES cell or a fertilized oocyte as claimed. Furthermore, necessary and enabling guidance appears to lacking from the instant specification as discussed in the previous office action dated 03/22/2005.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1,3,5-7,10 and 11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Deboer (1997, US 5,633,076; IDS) or Clark (1994, US 5,322,775;IDS) or Lubon (1998, US 5,831,141; IDS) in view of Morinaga (1983, PNAS, Vol. 80, pages 4604-4608; IDS) and Bennett (1997, Breast Cancer Research and Treatment, Vol. 45, pages 169-179; IDS) for reasons of record set forth at pages 10-13 of the previous office action dated 03/22/2005.

Applicant argues that neither Deboer, Clark nor Lubon teach or suggest the claimed subject matter. However, Applicant fails to point out which limitations are missing by DeBoer, Clark and Lubon that are not fulfilled by Morinaga. In response, it is maintained that all of the claim limitations are met by the combination of DeBoer, Clark, Lubon and Morinaga (see paragraph bridging pages 6-7 of the office action dated 10/31/2005).

Applicant argues that Bennett fails to provide motivation for combining the above-cited references. In response, Bennett provides support for an art-recognized need to produce large quantities of rHuAFP. That Bennett provides a means differing from that of the instant invention

for obtaining such large quantities of rHuAFP does not overcome the instant rejection. Furthermore, it is noted that AFP is well-known in the art to be a glycosylated protein and it is also well-known that proteins made using bacterial expression systems like that of Bennett are not post-translationally processed. More importantly, the folding of recombinant proteins in bacterial systems is often affected and the protein forms aggregates that must be solubilized and refolded prior to purification, a process that is not practical for large scale preparation (for example, see Clark, col. 1, lines 23-27; Bennett, page 170, col. 2, paragraph 2). Regardless of the success of using the *E. coli* system of Bennett, one of skill in the art would be motivated to use a mammalian system to obtain post-translationally processed forms of the protein or a source of the protein that does not need to undergo solubilization and refolding steps. Thus, with Bennett demonstrating a desire for one of skill in the art to obtain large quantities of rHuAFP and Clark, as well as DeBoer and Lubon, teaching a mammalian system as a means of overcoming shortcomings of a prokaryotic system in manufacturing large quantities of a protein, as exemplified by Bennett, one of skill in the would clearly have been motivated to carry out the claimed invention at the time the application was filed.

Thus, the claimed invention, as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER